REMARKS

A. Status of the Claims and Amendments

Claims 1-9 were filed in the instant application. Claims 2-5 stand objected to due to informalities. Claim 8 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claims 1-7 and 9 stand rejected under 35 U.S.C. §102(b) as being anticipated by Falk *et al.* (WO 91/04058). Claims 1-7 and 9 also stand rejected under 35 U.S.C. §102(e) and 35 U.S.C. §102(a) as being anticipated by Falk *et al.* (U.S. Patent 5,985,850). Claims 1, 6, 7, and 9 stand rejected under 35 U.S.C. §102(e) and 35 U.S.C. §102(a) as being anticipated by Turley *et al.* (U.S. Patent 6,475,795). Claim 8 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Falk *et al.* (U.S. Patent 5,985,850). The specific grounds for rejection and applicants' response to them are set forth in detail below.

Claim 2 and the specification have been amended at the suggestion of the examiner to correct informalities and expedite the prosecution of this application. Claims 1, 8, and 9 have been amended. Support for all amended claims is found within the specification. These amendments do not introduce new matter. Therefore, claims 1-9 are presented for reconsideration.

B. Rejection Under 35 U.S.C. § 112

Claim 8 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. According to the examiner, there is insufficient antecedent basis for the limitation "an effective amount of said agent" in claim 8 because the claim is directed to a method for the reduction of gastrointestinal toxicity of a drug, not of an agent. Claim 8 has been amended to

better state the invention. Applicants believe that these amendments should satisfy the examiner's concerns on this issue.

In view of this amendment, Applicants respectfully request that the rejection of claim 8 under 35 U.S.C. §112, second paragraph, be withdrawn.

C. **Rejection under 35 U.S.C. § 102(b) over Falk *et al.* (WO 91/04058)**

Claims 1-7 and 9 stand rejected under 35 U.S.C. §102(b) as being anticipated by Falk *et al.* (WO 91/04058). The Examiner contends that Falk discloses injectable formulations comprising an anti-cancer agent or chemotherapeutic agent and hyaluronic acid for the treatment of a disease or condition. Applicants traverse.

Applicants have amended the claims to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Falk, as all compositions administered by Falk contain hyaluronan with a molecular weight less than 750,000 Daltons. While the Examiner argues that Falk "contemplates the use of hyaluronic acid having greater molecular weight (See p. 33, lines 29-31)," it cannot be said that Falk specifically teaches any molecular weights greater than 750,000 Daltons. Anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1327, 58 U.S.P.Q.2d 1545, 1552 (Fed. Cir. 2001); *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Because Falk does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Falk does not teach each and every element of the claims as amended.

Accordingly, it is believed that the claims as amended are not anticipated by Falk. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

D. **Rejection under 35 U.S.C. § 102(e) over Falk *et al.* (U.S. Patent 5,985,850)**

Claims 1-7 and 9 stand rejected under 35 U.S.C. §102(e) as being anticipated by Falk *et al.* (U.S. Patent 5,985,850). The examiner contends that Falk discloses injectable formulations comprising an anti-cancer agent or chemotherapeutic agent and hyaluronic acid for the treatment of a disease or condition. Applicants traverse.

Applicants have amended the claims to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Falk, as all compositions administered by Falk contain hyaluronan with a molecular weight less than 750,000 Daltons. While the Examiner argues that Falk "contemplates the use of hyaluronic acid having greater molecular weight (see col. 19, lines 31-33)," it cannot be said that Falk specifically teaches any molecular weights greater than 750,000 Daltons. As noted above, anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. Because Falk does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Falk does not teach each and every element of the claims as amended.

Accordingly, it is believed that the claims as amended are not anticipated by Falk. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

E. **Rejection under 35 U.S.C. § 102(e) over Turley *et al.* (U.S. Patent 6,475,795)**

Claims 1, 6, 7, and 9 stand rejected under 35 U.S.C. §102(e) as being anticipated by Turley *et al.* (U.S. Patent 6,475,795). The examiner contends that Turley discloses pharmaceutical compositions comprising an anti-sense nucleic acid bound to hyaluronan for the treatment of a human suffering from a disease or condition treatable using gene therapy,

including tumors, and provides methods of targeting gene therapy in a human comprising administering said compositions by systemic administration. Applicants traverse.

Applicants have amended the claims to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Turley, as all compositions administered by Turley contain hyaluronan with a molecular weight less than 750,000 Daltons. While the Examiner argues that Turley "contemplates the use of higher molecular weight hyaluronans (See col. 10, lines 6-9)," it cannot be said that Turley specifically teaches any molecular weights greater than 750,000 Daltons. In fact, Applicants assert that a person of ordinary skill in the art would be discouraged from using higher molecular weight hyaluronans based on the teachings in Turley. At col. 10, lines 13-14, Turley states that "larger molecular weight hyaluronic acid should be avoided." As noted above, anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. Because Turley does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Turley does not teach each and every element of the claims as amended.

Accordingly, it is believed that the claims as amended are not anticipated by Turley. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

F. **Rejection under 35 U.S.C. § 102(a) over Falk *et al.* (U.S. Patent 5,985,850)**

Claims 1-7 and 9 stand rejected under 35 U.S.C. §102(a) as being anticipated by Falk *et al.* (U.S. Patent 5,985,850). The examiner contends that Falk discloses injectable formulations comprising an anti-cancer agent or chemotherapeutic agent and hyaluronic acid for the treatment of a disease or condition. Applicants traverse.

Applicants have amended the claims to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Falk, as all compositions administered by Falk contain hyaluronan with a molecular weight less than 750,000 Daltons. While the Examiner argues that Falk "contemplates the use of hyaluronic acid having greater molecular weight (See col. 19, lines 31-33)," it cannot be said that Falk specifically teaches any molecular weights greater than 750,000 Daltons. As noted above, anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. Because Falk does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Falk does not teach each and every element of the claims as amended.

Accordingly, it is believed that the claims as amended are not anticipated by Falk. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

G. Rejection under 35 U.S.C. § 102(a) over Turley *et al.* (U.S. Patent 6,475,795)

Claims 1, 6, 7, and 9 stand rejected under 35 U.S.C. §102(a) as being anticipated by Turley *et al.* (U.S. Patent 6,475,795). The examiner contends that Turley discloses pharmaceutical compositions comprising an anti-sense nucleic acid bound to hyaluronan for the treatment of a human suffering from a disease or condition treatable using gene therapy, including tumors, and provides methods of targeting gene therapy in a human comprising administering said compositions by systemic administration. Applicants traverse.

Applicants have amended the claims to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Turley, as all compositions administered by Turley contain hyaluronan with a molecular weight less than 750,000 Daltons. While the Examiner argues that Turley

"contemplates the use of higher molecular weight hyaluronans (See col. 10, lines 6-9)," it cannot be said that Turley specifically teaches any molecular weights greater than 750,000 Daltons. In fact, Applicants assert that a person of ordinary skill in the art would be discouraged from using higher molecular weight hyaluronans based on the teachings in Turley. At col. 10, lines 13-14, Turley states that "larger molecular weight hyaluronic acid should be avoided." As noted above, anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. Because Turley does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Turley does not teach each and every element of the claims as amended.

Accordingly, it is believed that the claims as amended are not anticipated by Turley. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

H. Rejection under 35 U.S.C. § 103(a) over Falk *et al.* (U.S. Patent 5,985,850)

Claim 8 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Falk *et al.* (U.S. Patent 5,985,850). The Examiner contends the only element of claim 8 not taught by Falk is that the method of the invention reduces gastrointestinal toxicity of a drug, but the Examiner argues that gastrointestinal toxicity is one of the most common side effects experienced by patients taking chemotherapeutic agents. Thus, the Examiner argues that because Falk provides the general teachings that the compositions of the inventions are non-toxic, provide no adverse effect, and help the body eliminate toxins, it would be expected that administration of said composition would reduce gastrointestinal toxicity as compared to the effect of compositions comprising the chemotherapeutic agent alone. Applicants traverse.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the

knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. *Manual of Patent Examining Procedure* §2142. See also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991) (emphasizing that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be both found in the prior art, and not based on applicant's disclosure). It is important to note that all three elements must be shown to establish a *prima facie* case of obviousness. Thus, if even one element is missing, a *prima facie* case of obviousness does not exist.

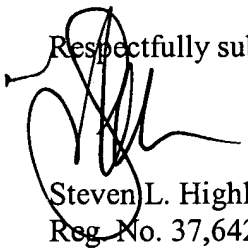
The first step in establishing a *prima facie* case of obviousness is presenting evidence that Falk teaches or suggests all of the claim limitations of Applicants' present claims. While Applicants content that Falk fails to teach or suggest all the claim limitations of original claim 8, in the interest of advancing prosecution, Applicants have amended claim 8 to recite that the hyaluronan must have a molecular weight greater than or equal to about 750,000 Daltons. This amendment clearly distinguishes the current claims from Falk, as all compositions administered by Falk contain hyaluronan with a molecular weight less than 750,000 Daltons. Because Falk does not disclose the use of hyaluronans with a molecular weight greater than or equal to about 750,000 Daltons, Falk does not teach each and every element of claim 8 as amended. Moreover, as discussed above, Turley (col. 10, lines 13-14) states that "larger molecular weight hyaluronic acid should be avoided," thereby leading one of skill in the art ***away*** from higher molecular weight species. Thus, Falk fails to establish a necessary element required for a *prima facie* case of obviousness.

Because the examiner has failed to present a *prima facie* case of obviousness on at least one of the three elements, Applicants respectfully request that the rejection of claim 8 be withdrawn.

I. Conclusion

Applicants have submitted arguments that are believed to overcome all outstanding rejections. Therefore, allowance of this application is solicited. In the event that the Examiner has suggestions regarding claim amendments or additional information that might speed this case toward allowance, the Examiner is requested to contact the Applicants' representative listed below.

Respectfully submitted,



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